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L1: Entry 2 of 4 File: USPT Aug 18, 1992

DOCUMENT-IDENTIFIER: US 5139803 A
TITLE: Method and liposome composition for the stabilization of oxidizable substances

Abstract Text (1):
A stable, food-compatible liposome is prepared by dissolving a lipophilic material in a phospholipid followed by the addition of water or an aqueous solution and mixing by sonicating to produce a liposome having the lipophilic material encapsulated in the lipid bilayer. The preferred lipophilic materials include any readily oxidizable lipid and in particular the omega-3 fatty acid containing fish oils. Other lipophilic materials which can be encapsulated in the lipidic bilayer include flavorants, acidulants, preservatives and antioxidants. The resulting liposomes provide a stabilizing vehicle for the lipophilic materials to reduce the occurrence of oxidation and rancidity. Liposomes prepared according to the disclosed method exhibit none of the unpleasant odor and flavor characteristics normally associated with oxidized or rancid oils. The liposomes provide an extended shelf life of the unstable oils and can be added directly to the food product as a dispersion during the manufacturing stage or dried to a free flowing powder for later use.

Brief Summary Text (3):
The present invention relates to the production of liposomes containing lipophilic materials dissolved in the lipid layer of the liposome. More specifically, the invention is directed to the stabilization of oxidizable unsaturated lipophilic compounds by the encapsulation of the material in the lipidic layer of a liposome to retard or inhibit oxidation. The invention further relates to a lipophilic material stabilized by encapsulating the material in a liposome having a predetermined thermal transition temperature and shear resistance to withstand the physical treatments normally encountered in commercial food preparation. The liposomes can be used to introduce a readily oxidizable lipidic component to foods in a pure form. The liposomes offer a means whereby the lipophilic component can be easily dispersed in an aqueous phase. The liposomes can also be introduced to food compositions to slowly release the material dissolved in the lipidic layer over an extended period of time.

Brief Summary Text (29):
The present invention is therefore directed to a food-compatible liposome composition containing highly oxidizable lipophilic materials dissolved in the lipid layer of a liposome. The liposomes prepared according to the invention provide a means to prevent or inhibit oxidation of the encapsulated lipophilic material. The invention is further directed to a suitable lipid-containing food product containing large amounts of the novel liposome composition but free from adverse effects on its flavor and odor.

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L2: Entry 20 of 28 File: USPT Dec 31, 1996

DOCUMENT-IDENTIFIER: US 5589189 A
TITLE: Liposome dispersion

Brief Summary Text (7):
Liposomes are microscopic vesicles made from phospholipids, which form closed, fluid filled spheres when dispersed with aqueous solutions. Phospholipid molecules are polar, having a hydrophilic head and two hydrophobic tails consisting of long fatty acid chains. Thus, when a sufficient concentration of phospholipid molecules are present in aqueous solutions, the mils spontaneously associate to exclude water while the hydrophilic phosphate heads interact with water. The result is a spherical, bilayer membrane in which the fatty acid tails converge in the interior of the newly formed membrane, and the polar heads point in opposite directions toward an aqueous medium. These bilayer membranes thus form closed, hollow spheres known as liposomes. The polar heads at the inner surface of the membrane point toward the aqueous interior of the liposome and, at the opposite surface of the spherical membrane, the polar heads interact with the surrounding aqueous medium. As the liposomes are formed, water soluble molecules can be incorporated into the aqueous interior, and lipophilic molecules may be incorporated into the lipid bilayer. Liposomes may be either multilamellar, like an onion with liquid separating many lipid bilayers, or unilamellar, with a single bilayer surrounding an aqueous center.

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L2: Entry 19 of 28 File: USPT Aug 12, 1997

DOCUMENT-IDENTIFIER: US 5656287 A
TITLE: Liposomal cyclosporin formulations as agents for immunosuppression and multiple drug resistant indications

Brief Summary Text (10):
Efforts have been made to eliminate the toxicity of cyclosporine by incorporating the drug into liposomes for purposes of administration, thus eliminating the toxic castor oil vehicle. Liposomes are microscopic delivery vesicles made, in part, from phospholipids which form closed, fluid filled spheres when mixed with water. Phospholipid molecules are polar, having a hydrophilic ionizable head, and a hydrophobic tail consisting of long fatty acid chains. Thus, when sufficient phospholipid molecules are present with water, the tails spontaneously associate to exclude water while the hydrophilic phosphate heads interact with water. The result is a bilayer membrane in which the fatty acid tails converge in the newly formed membrane's interior and the polar heads point in opposite directions toward an aqueous medium. The polar heads at one surface of the membrane point toward the aqueous interior of the liposome. At the opposite surface, the polar heads interact with the surrounding aqueous medium. As the liposomes form, water soluble molecules will be incorporated into the aqueous interior, and lipophilic molecules will tend to be incorporated into the lipid bilayer. Liposomes may be either multilamellar, like an onion with liquid separating many lipid bilayers, or unilamellar, with a single bilayer surrounding an entirely liquid center.

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L5: Entry 6 of 38 File: USPT Mar 23, 1999

US-PAT-NO: 5885564
DOCUMENT-IDENTIFIER: US 5885564 A

TITLE: Functional oxygenated composition containing phospholipids and fluorocarbon

DATE-ISSUED: March 23, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Golz; Karin	Monaco			MC
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US-CL-CURRENT: 424/74; 424/195.16, 424/195.17, 424/727, 424/744, 424/757, 424/78.02, 424/78.03

CLAIMS:

What is claimed is:

1. Functional oxygenaceous preparation, comprising a content of

(a) from 0.1% to 50% by weight of phospholipids and an oxygen laden fluorocarbon or fluorocarbon mixture, which is emulsified to produce a fluorocarbon emulsion, said fluorocarbon content being in the range of 0.2% to 100% weight/volume of said emulsion, and comprising a lipid fraction having a phosphatidylcholine content of 30% to 99% by weight, said emulsion and said lipid fraction forming asymmetrical lamellar aggregates, having a skin penetration which is a function of the critical solubility temperature of the fluorocarbon;

wherein the fluorocarbon is selected from the group consisting of aliphatic straight chain fluoroalkanes, branched chain fluoroalkanes, monocylic fluorocycloalkanes, bicyclic fluorocycloalkanes, optionally fluoroalkyl substituted fluorocycloalkanes, perfluorinated aliphatic amines, perfluorinated bicylic amines, bis-(perfluoroalkyl)-ethenes, and the mixtures thereof;

(b) from 0.1% to 50% by weight of a digestive treatment product obtained by a mild digestive treatment by means of ultrasonic or high pressure homogenization up to 25 MPa or both methods, of suspensions or dispersions of cells selected from the group consisting of vegetable matter, bacteria and yeasts, said product selected from the group consisting of proteins, peroxide dismutase, enzymes, nucleic acids, vitamins, fluoroanoides, and hormones; and

(c) the balance up to 100% by weight of a carrier substance suitable for application to the skin; and

with each percent by weight based upon the total preparation weight; and

said preparation having increased oxygen content due to the presence of said digestive treatment product.

2. A preparation according to claim 1,

wherein the yeast is selected from the group consisting of bakers' yeast, brewers' yeast, wine yeast, and yeast enriched with peroxide dismutase.

3. A preparation according to claim 1,

wherein the vegetable matter is the bark of the Mexican skin tree, (Mimosa tenuiflora).

4. A preparation according to claim 1,

wherein the vegetable matter is selected from the group consisting of green algae, seeds, grains, barks, and plant extracts.

5. A preparation according to claim 1,

wherein the digestive treatment product further contains at least one substance selected from the group consisting of proteins, Aloe vera, rosemarine, and camomile.

6. A preparation according to claim 1,

wherein the digestive treatment product further contains a combination of fruit acids selected from the group consisting of malic acid, citric acid, tartaric acid, fumaric acid, succinic acid, gluconic acid, and lactic acid.

7. A preparation according to claim 1,

wherein the digestive treatment product further contains vitamins comprising the vitamin combinations selected from the group consisting of P-B-A, A-E-C, and B-E-A.

8. A preparation according to claim 1,

wherein the fluorocarbons are selected from the group consisting of perfluorodecalin, F-butyltetrahydrofuran, perfluorotributylamine, perfluorooctylbromide, bisfluoro (butyl) ethene and C.sub.6 -C.sub.9 - perfluoroalkanes, and the mixtures thereof.

9. A preparation according to claim 1,

wherein the proportion of fluorocarbons is in the range of 20% to 100% w/v, in the fluorocarbon emulsion, which is added to the lipid fraction.

10. A preparation according to claim 1,

wherein the proportion of fluorocarbons is in the range of 40% to 100% w/v, in the fluorocarbon emulsion which is added to the lipid fraction.

11. A preparation according to claim 1,

wherein the fluorocarbon aggregates of (a) range from 0.5% to 45% by weight;

wherein the digestive treatment product of (b) range from 0.5% to 40% by weight; and

the balance up to 100% by weight is the carrier substance of (c).

12. A preparation according to claim 1,

wherein the fluorocarbon aggregates of (a) range from 10% to 40% by weight;

wherein the digestive treatment product of (b) range from 1% to 10% by weight; and

the balance up to 100% is the carrier substance of (c).

13. Process for the manufacture of a functional oxygenaceous preparation, comprising the steps of

(a) treating suspensions of dispersions of cells of vegetable matter, bacteria or yeasts digestively by mild ultrasonic treatment or high pressure homogenization up to 25 MPa, or both methods to produce a digestive treatment product selected from the group consisting of proteins, peroxide dismutase, enzymes, nucleic acids, vitamins, fluoranoides, and hormones;

(b) emulsifying a lipid fraction containing phospholipids with an oxygen-laden fluorocarbon emulsion comprising a fluorocarbon or fluorocarbon mixture in an aqueous medium, the fluorocarbon content in the fluorocarbon emulsion being in the range of 0.2% to 100% weight/volume and the content of phosphatidylcholine in the lipid fraction amounting to 30% to 99t by weight;

wherein the fluorocarbon is selected from the group consisting of aliphatic straight chain fluoroalkanes, branched chain fluoroalkanes, monocylic fluorocycloalkanes, bicyclic fluorocycloalkanes, optionally fluoroalkyl substituted fluorocycloalkanes, perfluorinated aliphatic amines, perfluorinated bicylic amines, bis-(perfluoroalkyl)-ethenes, and the mixtures thereof;

(c) mixing the digestive treatment product of (a) with the emulsion of (b) to produce asymmetrical lamellar aggregates and;

(d) incorporating the asymmetrical lamellar aggregates obtained by (c) which incorporate the digestive treatment product of (a) in a carrier substance suitable for application to skin;

said asymmetrical lamellar aggregates being from 0.1% to 50% by weight of the preparation;

said digestive treatment product being from 0.1% to 50% by weight of the preparation; and

said carrier being the balance up to 100% by weight;

with all percents by weight being based upon the total preparation weight; and

said preparation having increased oxygen content due to the presence of said digestive treatment product.

14. Process according to claim 13, comprising

obtaining the digestive treatment product by an ultrasonic digestive treatment using an ultrasonic continuous flow cell in which the synotrode projects as to 1/2 to 2/3 its length into the continuous flow cell, the angle of the synotrode in the sound exposure vessel being in the range of 80.5.degree. to 88.5.degree., the ratio of immersion length of the synotrode (in mm) to the sound irradiated volume (in ml) being set to a value in the range of 1:1.1 to 1:20 and the ratio of immersion length of the synotrode (in mm) to a solids content of the medium to be irradiated ultrasonically (in weight %) being in the range of 0:0.02 to 1:2.2.

15. Process according to claim 14,

wherein the solids concentration present in the medium to be subjected to ultrasonic treatment is in the range of 0.5 to 65 weight %.

16. Process according to claim 13,

wherein particle size of the asymmetrical lamellar aggregates is in the range of 50 to 1000 nm.

17. Process according to claim 13,

wherein particle size of the asymmetrical lamellar aggregates is in the range of 120 to 820 nm.

18. Process according to claim 13,

wherein particle size of the asymmetrical lamellar aggregates is in the range of 140 to 400 nm.

19. Process according to claim 13,

wherein the fluorocarbon aggregates of (a) range from 0.5% to 45% by weight;

wherein the digestive treatment product of (b) range from 0.5% to 40% by weight; and

the balance up to 100% by weight is the carrier substance of (c).

20. Process according to claim 13,

wherein the fluorocarbon aggregates of (a) range from 10% to 40% by weight;

wherein the digestive treatment product of (b) range from 1% to 10% by weight; and

the balance up to 100% is the carrier substance of (c).

21. A cosmetic or dermatological functional oxygenaceous preparation, comprising

(a) from 0.1% to 50% by weight of phospholipids and an oxygen laden fluorocarbon or fluorocarbon mixture which is emulsified to produce a fluorocarbon emulsion, the proportion of fluorocarbon being in the range of 0.2% to 100% weight/volume of said emulsion, and comprising a lipid fraction having a phosphatidylcholine content of 30% to 99% by weight and said emulsion and said lipid fraction forming asymmetrical lamellar aggregates;

wherein the fluorocarbon is selected from the group consisting of aliphatic straight chain fluoroalkanes, branched chain fluoroalkanes, monocylic fluorocycloalkanes, bicyclic fluorocycloalkanes, optionally fluoroalkyl-substituted fluorocycloalkanes, perfluorinated aliphatic amines, perfluorinated bicylic amines, bis-(perfluoroalkyl)-ethenes, and the mixtures thereof;

(b) from 0.1% to 50% by weight of a digestive treatment product obtained by the mild digestive treatment by means of ultrasonic or high pressure homogenization up to 25 MPa or both methods, of suspensions or dispersions of cells of vegetable matter, bacteria or yeasts, said product selected from the group consisting of proteins, peroxide dismutase, enzymes, nucleic acids, vitamins, fluoroanoides, and hormones; and

(c) the balance up to 100% by weight of a carrier substance suitable for application to skin for the simultaneous supply of the skin with oxygen and with at least one substance selected from the group consisting of nutrients, active substances, protective agents and pharmaceutically active substances for the skin and the tissue underneath the skin;

with all percents by weight being based upon the total preparation weight; and

said preparation having increased oxygen content due to the presence of said digestive treatment product.

22. The cosmetic or dermatological functional oxygenaceous preparation according to claim 21,

wherein said substance (c) is selected from the group consisting of skin-care agents, sun protection formulations with UV absorbers, tanning agents, fat replenishing after-shaves, cleansing lotions and oils, encapsulated radical capturing agents, formulations against pregnancy stretch marks, hair and scalp care agents, bath oils, fitness friction agents, dermatological formulations with or without further pharmaceutically active substances.

23. A preparation according to claim 21,

wherein the fluorocarbon aggregates of (a) range from 0.5% to 45% by weight;

wherein the digestive treatment product of (b) range from 0.5% to 40% by weight; and

the balance up to 100% by weight is the carrier substance of (c).

24. A preparation according to claim 21,

wherein the fluorocarbon aggregates of (a) range from 10% to 40% by weight;

wherein the digestive treatment product of (b) range from 1% to 10% by weight; and

the balance up to 100% is the carrier substance of (c).

25. A preparation according to claim 21, comprising a face and body emulsion which consists essentially of

3.5% by weight of C12-15 alkyl benzoate;

3.0% by weight of Steareth-2.RTM.;

1.9% by weight of Steareth-21.RTM.;

2.5% by weight of caprylic/capric triglyceride PEG-4 esters;

q.s. distilled water;

0. 4% by weight of acrylates and C10-C30 alkyl acrylate crosspolymer;

0.4% by weight of triethanolamine;

1.5% by weight of Jojoba oil;

1.0% by weight of Babassu oil;

0.5% by weight of Vitamin E;

0.3% by weight of Preservative;

0.1% by weight of fluorocarbon aggregates;

0.1% by weight of yeast extract; and

0.3% by weight of perfume.

26. A preparation according to claim 21, comprising

a face and eye cleansing milk which consists essentially of

1.5% by weight of Steareth-2.RTM.;

1. 5% by weight of caprylic/capric triglyceride PEG-4 esters; 2.0% by weight of Calendula oil;

q.s. distilled water;

0.5% by weight of Carbomer.RTM.;

0.4% by weight of triethanolamine;

0.5% by weight of fluorocarbon aggregates;

2.0% by weight of Green algae extract; and

0.3% by weight of preservative.

27. A preparation according to claim 21, comprising

an anti-wrinkle mask which consists essentially of

2.8% by weight of cetearyl alcohol;

1.8% by weight of octyl stearate;

1.0% by weight of dicaprylyl ether;

q.s. distilled Water;

0. 4% by weight of acrylates and C10-C30 alkyl acrylate crosspolymer;

0.4% by weight of triethanolamine;

5.6% by weight of kaolin;

1.2% by weight of Vitamin E;

0.4% by weight of preservative;

2.0% by weight of Babassu oil;

1.0% by weight of Palm oil;

45.0% by weight of fluorocarbon aggregates;

10.0% by weight of yeast extract; and

0.3% by weight of perfume oil.

28. A preparation according to claim 21, comprising

a heparin ointment which consists essentially of

q.s. Distilled water;

1. 0% by weight of heparin;

2.0% by weight of Carbomer;

2.0% by weight of sodium hydroxide;

9.0% by weight of phospholipid;

20% by weight of perfluorodecalin;

7.0% by weight of fluroocarbon aggregates;

2.0% by weight of yeast extract; and

0.1% by weight of preservative.

29. A preparation according to claim 21, comprising

an ointment with acetylsalicylic acid which consists essentially of q.s. distilled water;

1.0% by weight of acetylsalicylic acid;

8.0% by weight of glycerin;

6.0% by weight of propylene glycol;

1. 0% by weight of ethanol;

4.5% by weight of phospholipid;

40.0% by weight of fluorocarbon aggregates; and

1.0% by weight of yeast extract.

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L5: Entry 19 of 38 File: USPT Nov 11, 1997

US-PAT-NO: 5686102
DOCUMENT-IDENTIFIER: US 5686102 A
** See image for Certificate of Correction **

TITLE: Pharmacological composition for topical administration

DATE-ISSUED: November 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gross; Udo	Berlin			DE
Roding; Joachim	Wiesbaden			DE
Stanzl; Klaus	White Plains	NY		
Zastrow; Leonhard	Monaco			MC

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 424/401, 514/944, 514/969

CLAIMS:

We claim:

1. Pharmaceutical composition for topical administration, comprising

asymmetric lamellar aggregates, comprising phospholipids having a phosphatidylcholine content of 30% to 99% by weight, pharmacological active compounds and fluorocarbon, the amount of fluorocarbon being in the range from 1% to 100% weight/volume, in a pharmaceutical excipient suitable for topical administration; and

said asymmetric lamellar phospholipid aggregates comprising a central core of fluorocarbons surrounded by at least three layers of phospholipid molecules wherein the layer adjacent to said central core has the lipophilic moiety of the phospholipid interact with the fluorocarbon.

2. Composition according to claim 1,

wherein the lamellar aggregates have an asymmetric 3-layer structure originating from their fluorocarbon core.

3. Composition according to claim 1,

wherein the fluorocarbon is selected from the group consisting of aliphatic straight-chain fluoroalkanes, aliphatic branched fluoroalkanes, monocyclic fluorocycloalkanes, monocyclic fluoroalkyl-substituted fluorocycloalkanes, bicyclic fluorocycloalkanes, bicyclic fluoroalkylsubstituted fluorocycloalkanes, perfluorinated aliphatic amines, perfluoroinated bicyclic amines, bis(perfluoroalkyl) ethenes, and mixtures thereof.

4. Composition according to claim 3,

wherein the fluorocarbon is selected from the group consisting of perfluorodecalin, F-butyltetrahydrofuran, perfluorotributylamine, perfluorooctyl bromide, bis-fluoro(butyl)ethene and C.sub.6 -C.sub.9 - perfluoroalkanes.

5. Composition according to claim 1,

wherein the amount of fluorocarbon is in the range from 20% to 100% weight/volume.

6. Composition according to claim 1,

wherein the amount of fluorocarbon is in the range from 40% to 100% weight/volume.

7. Composition according to claim 1,

wherein the amount of fluorocarbon is in the range from 70% to 100% weight/volume.

8. Composition according to claim 1,

wherein the phospholipids are selected from the group consisting of natural phospholipids, synthetic phospholipids, and the mixtures thereof in a concentration between 0.5% and 20%.

9. Composition according to claim 1,

wherein phosphatidylcholine is present in an amount from 70% to 90% by weight.

10. Composition according to claim 1,

wherein the lipid fraction used, in addition to phosphatidylcholine, lysolecithins are present in the concentration range from 1% to 5% by weight.

11. Composition according to claim 1,

wherein there is a pharmocological active compound selected from the group consisting of dermatological active compounds, systemic active compounds, and mixtures thereof.

12. Composition according to claim 11,

wherein the pharmacological active compound is a pharmaceutical selected from the group consisting of virustatics, virucidal pharmaceuticals, antimycotics, heparins, antibiotics, corticoids, antiinfectious agents, anti-acne compounds, local anesthetics, antiinflammatories, antihistamines, antipsoriatic agents, and the mixtures thereof.

13. Composition according to claim 11,

wherein the systemic active compound is a pharmaceutical selected from the

group consisting of the non-steroidal analgesics, antirheumatics, opiate receptor agonists, opiate receptor antagonists, heparins, histamine antagonists, insulins, regulatory peptides, sedative and hypnotics.

14. Composition according to claim 11,

wherein the dermatological active compound is a virucidal active compound.

15. Composition according to claim 13,

wherein the systemic active compound is a low molecular weight heparin, a high molecular weight heparin, an oligopeptide or a polypeptide.

16. Process for the preparation of a phospholipid-containing pharmaceutical composition comprising the steps of

emulsifying phospholipids having a phosphatidylcholine content of 30% to 99% by weight with a fluorocarbon or fluorocarbon mixture, a pharmacological active compound or an active compound combination being incorporated into the emulsion, and the amount of fluorocarbon being in the range from 1 to 100 per cent weight/volume to produce asymmetric lamellar aggregates; and

incorporating the asymmetric lamellar aggregates obtained in this way into an excipient suitable for topical administration as active compound carriers having a particle size from 50 nm to 1000 nm; and

said asymmetric lamellar phospholipid aggregates comprising a central core of fluorocarbons surrounded by at least three layers of phospholipid molecules wherein the layer adjacent to said central core has the lipophilic moiety of the phospholipid interact with the fluorocarbon.

17. Process according to claim 16,

wherein the amount of fluorocarbon is in the range from 20% to 100% by weight/volume; and

the amount of phosphatidylcholine in the phospholipid is in the range from 70% to 90% by weight.

18. Process according to claim 16,

wherein the amount of fluorocarbon is in the range from 40% to 100% by weight/volume.

19. In a method for the topical application of a pharmaceutical composition,

the improvement comprising topically applying a system containing phospholipids having a phosphatidylcholine content of 30% to 99% by weight, pharmacological active compounds and fluorocarbons in the form of asymmetric lamellar aggregates;

the fluorocarbon content being in the range from 0.2% to 100% weight/volume; and

the system being present for topical administration in a carrier selected from

the group consisting of ointment, cream, lotion, paste, gel, powder a dressing, a plaster, and a spray; and

said asymmetric lamellar phospholipid aggregates comprising a central core of fluorocarbons surrounded by at least three layers of phospholipid molecules wherein the layer adjacent to said central core has the lipophilic moiety of the phospholipid interact with the fluorocarbon.

20. Composition according to claim 11,

wherein there is a pharmaceutical active compound selected from the group consisting of a cytostatic, a cancerostatic, an immunodulator, a vaccine, and mixtures thereof.

21. Composition according to claim 14,

wherein the dermatological active compound is rosmarinic acid.

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